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(12) **United States Patent**
Barzaghi et al.(10) **Patent No.:** **US 7,115,780 B2**
(45) **Date of Patent:** **Oct. 3, 2006**(54) **PROPANOLAMINOMETHYLTETRALINES,
THEIR PREPARATION AND
PHARMACEUTICAL COMPOSITION
COMPRISING SAME**(75) Inventors: **Laura Barzaghi**, Monza (IT); **Roberto Cecchi**, Lodi (IT); **Nunzia Viviani**, Cantu (IT)(73) Assignee: **Sanofi-Aventis**, Paris (FR)

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(21) Appl. No.: **10/497,379**(22) PCT Filed: **Dec. 2, 2002**(86) PCT No.: **PCT/FR02/04129**§ 371 (c)(1),
(2), (4) Date: **Jun. 2, 2004**(87) PCT Pub. No.: **WO03/048117**PCT Pub. Date: **Jun. 12, 2003**(65) **Prior Publication Data**

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C07C 307/02 (2006.01)
C07D 263/52 (2006.01)
C07D 265/36 (2006.01)
A61K 31/18 (2006.01)
A61K 31/42 (2006.01)(52) **U.S. Cl.** **564/308**; 564/99; 564/399;
548/217; 544/105; 514/230.5; 514/375; 514/605;
514/647(58) **Field of Classification Search** None
See application file for complete search history.(56) **References Cited****U.S. PATENT DOCUMENTS**4,004,028 A 1/1977 Kaiser
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2004/0034070 A1 * 2/2004 Barzaghi et al. 514/357**FOREIGN PATENT DOCUMENTS**EP 0 375 560 A1 12/1989
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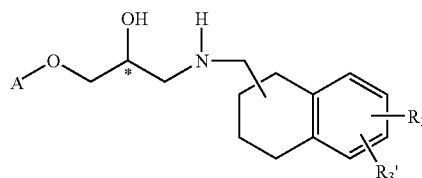
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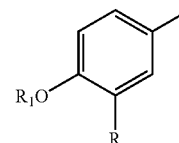
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(57) **ABSTRACT**

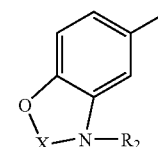
The invention concerns compounds of formula (I), wherein A is a group of formula (a) or (b), wherein: R represents a hydrogen or halogen atom, a $-\text{S}(\text{O})_z(\text{C}_1-\text{C}_4)\text{Alk}$ wherein z is 0, 1 or 2, a $-\text{NHSO}_2(\text{C}_1-\text{C}_4)\text{Alk}$, $-\text{SO}_2\text{NH}(\text{C}_1-\text{C}_4)\text{Alk}$, $-\text{NHSO}_2-(\text{C}_1-\text{C}_4)\text{Alk-phenyl}$ or $-\text{NHSO}_2\text{-phenyl}$ group, said phenyl capable of bearing a halogen atom, a $(\text{C}_1-\text{C}_4)\text{Alk}$ group or a $(\text{C}_1-\text{C}_6)\text{alkoxy}$ group; R_1 represents a hydrogen atom or a $-(\text{C}_1-\text{C}_4)\text{Alk}$, $-\text{CO}(\text{C}_1-\text{C}_4)\text{Alk}$, $-(\text{C}_1-\text{C}_4)\text{Alk-phenyl}$ or $-\text{CO-phenyl}$ group, said phenyl capable of bearing a halogen atom or a $-(\text{C}_1-\text{C}_4)\text{Alk}$ or $(\text{C}_1-\text{C}_6)\text{alkoxy}$ group; R_2 is a hydrogen atom, a $-\text{SO}_2(\text{C}_1-\text{C}_4)\text{Alk}$, $-\text{SO}_2-(\text{C}_1-\text{C}_4)\text{Alk-phenyl}$, $-\text{SO}_2\text{-phenyl}$ group, or a $-(\text{C}_1-\text{C}_4)\text{Alk}$ group; X completes a saturated or unsaturated cycle of 5 to 8 atoms, capable of bearing one or two $-(\text{C}_1-\text{C}_4)\text{Alk}$ groups and/or two carbonyl groups; R_3 and R_3' represent each independently a hydrogen or halogen atom, a $-(\text{C}_1-\text{C}_6)\text{Alk}$, hydroxy, $-\text{CN}$, $-(\text{C}_1-\text{C}_6)\text{alkoxy}$, $-\text{COR}_4$ or $\text{Y}-\text{CR}_8\text{R}_9-\text{COR}_4$ group; Y represents O or CH_2 ; R_4 represents a hydroxy, $(\text{C}_1-\text{C}_6)\text{alkoxy}$ or $-\text{NR}_5\text{R}_6$ group; R_5 and R_6 independently represent a hydrogen atom, a $-(\text{C}_1-\text{C}_4)\text{Alk}$, group, aryl or heteroaryl optionally substituted by a R_7 group, aralkyl or heteroaralkyl optionally substituted by a R_7 group; or R_5 and R_6 , with the nitrogen atom which bears them, form a saturated or unsaturated cycle of 5 to 7 atoms optionally substituted by a R_7 group; and R_7 represents a hydrogen or halogen atom, a hydroxy, $-(\text{C}_1-\text{C}_4)\text{Alk}$, $-(\text{C}_1-\text{C}_6)\text{alkoxy}$, $-\text{NH}(\text{C}_1-\text{C}_4)\text{Alk}$, $-\text{N}(\text{C}_1-\text{C}_4)\text{Alk}_2$, $-\text{COO}(\text{C}_1-\text{C}_4)\text{Alk}$, aralkyl or heteroaryl group; R_8 and R_9 independently represent a hydrogen atom or a $-(\text{C}_1-\text{C}_4)\text{Alk}$ group; their salts or solvates, the pharmaceutical compositions containing them, a method for preparing them and synthesis intermediates



(I)



(a)



(b)

23 Claims, No Drawings